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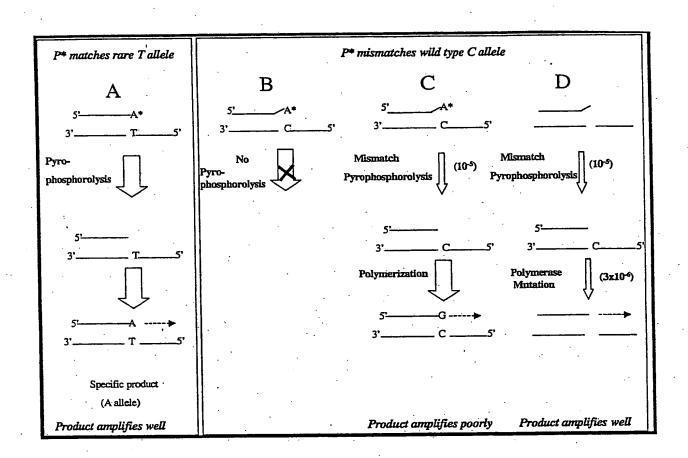


FIG. 1

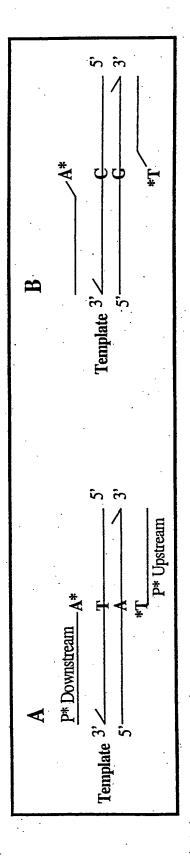


FIG. 2

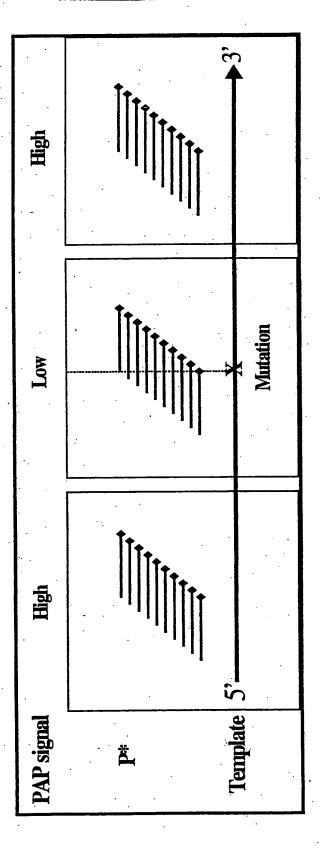
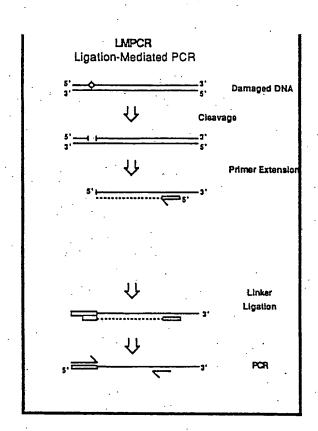


FIG. 3

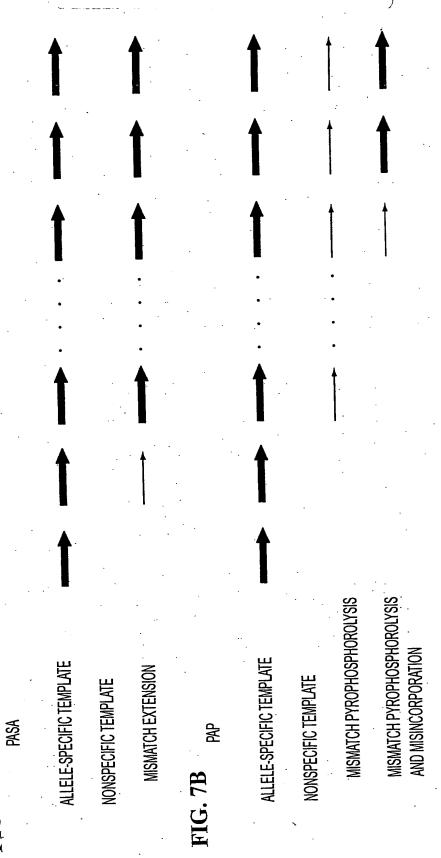
A. Wild type sample 5'-3' sense strand of the wild type sequence "CITGCTTGGAACTTGAGGGGGTGTCAG
PAP signal with dye-labeled dideoxynucleoside triphosphates  ddA**ddA  ddG**ddC  ddC**ddC
Base calling: wild type template  " C T G C T T G G A A C T T G G G G T C A G   B. G-A mutation
ddA*-ddA         ***         **
Sase calling: G-A mutation

FIG. 4



**FIG. 5** 





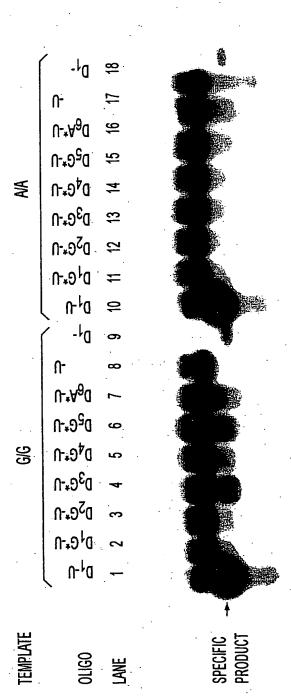
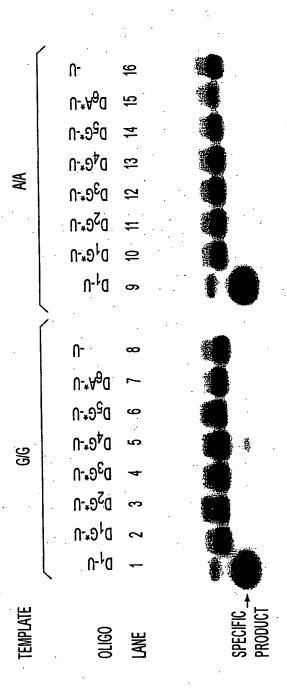
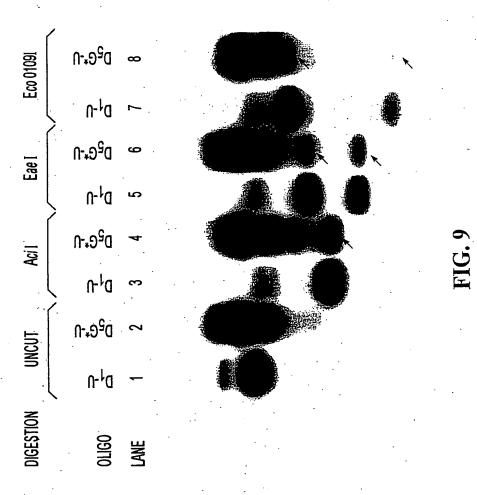
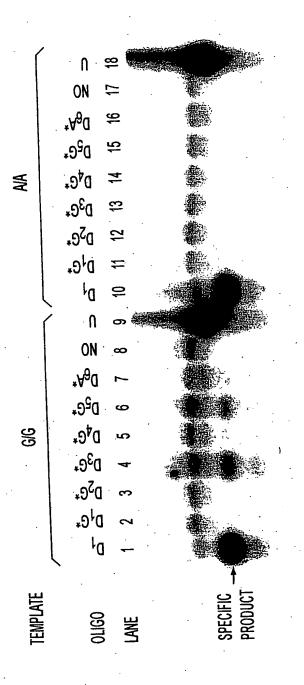


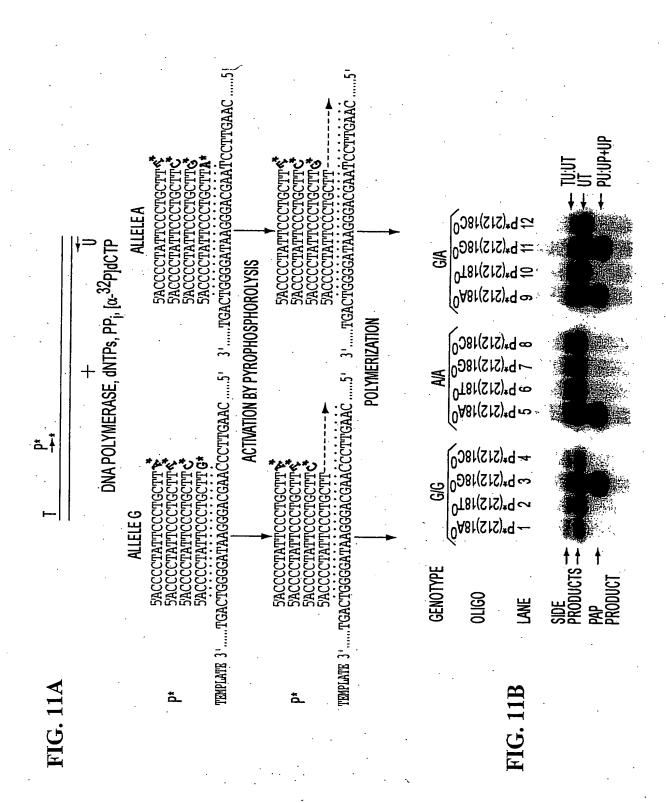
FIG. 8A

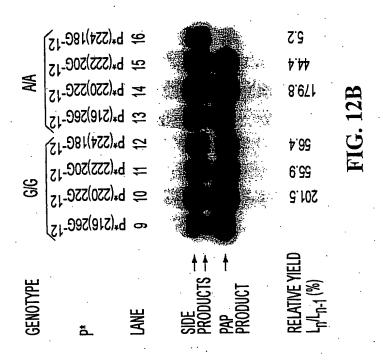


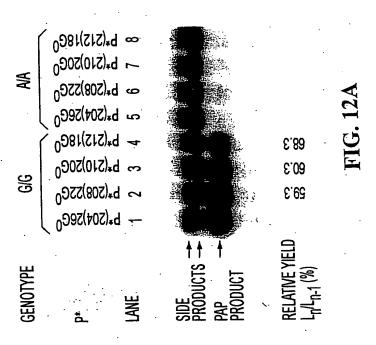
IG. 8B

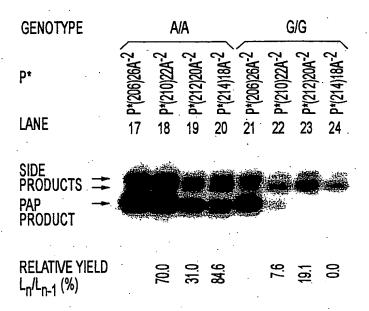










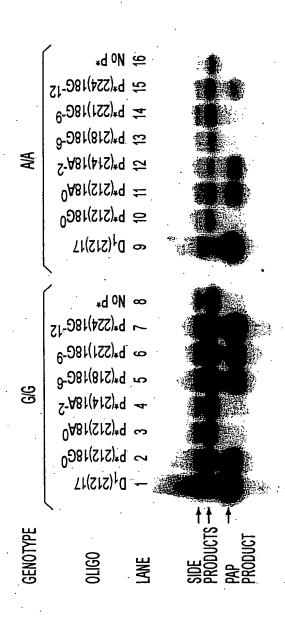


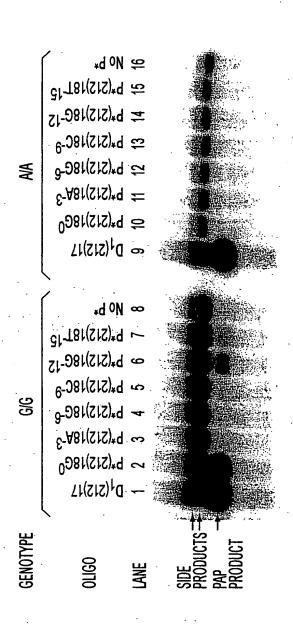
**FIG. 12C** 

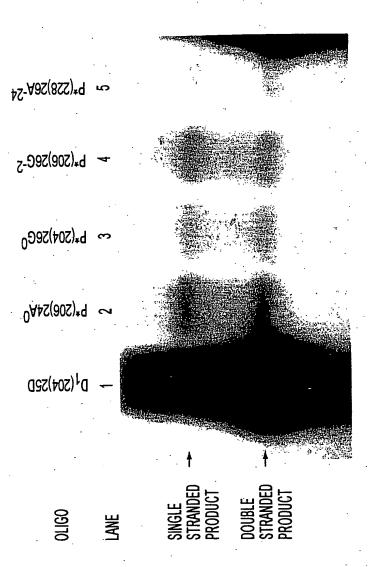
GENOTYPE	A/A .	GENOTYPE	A/A
P*	P*(206)26G <sup>-9</sup> P*(210)22G <sup>-9</sup> P*(212)20G <sup>-9</sup> P*(214)18G <sup>-9</sup>	<b>p</b> *	P*(206)26T <sup>-15</sup> P*(210)22T <sup>-15</sup> P*(212)20T <sup>-15</sup> P*(214)18T <sup>-15</sup>
LANE	25 26 27 28	LANE	29 30 31 32
SIDE PRODUCTS == PAP == PRODUCT		SIDE PRODUCTS = PAP PRODUCT	
RELATIVE YIELI L <sub>n</sub> /L <sub>n-1</sub> (%)	64.8 17.5 8.0	RELATIVE YIEI L <sub>n</sub> /L <sub>n-1</sub> (%)	37.6 2.2 0.0

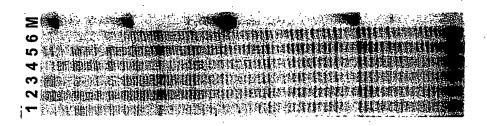
**FIG. 12D** 

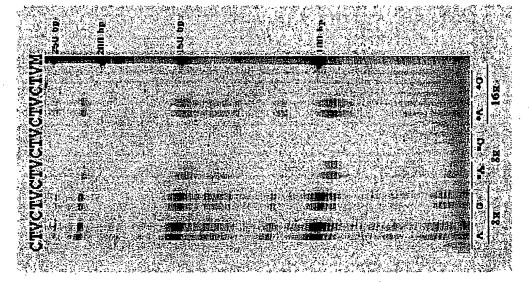
FIG. 12E





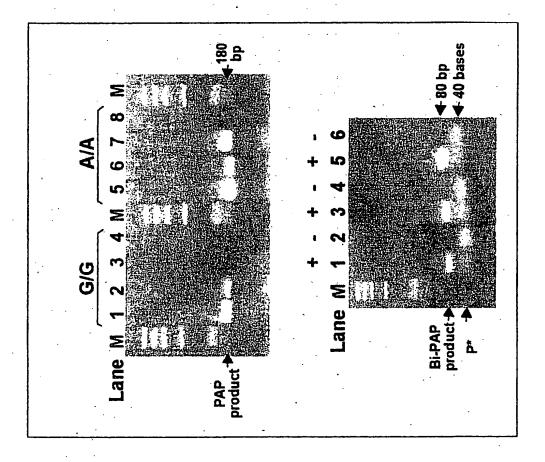




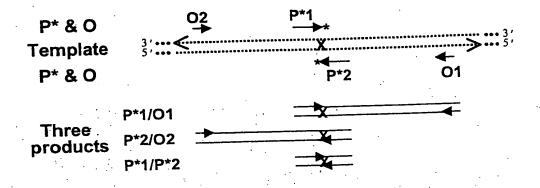




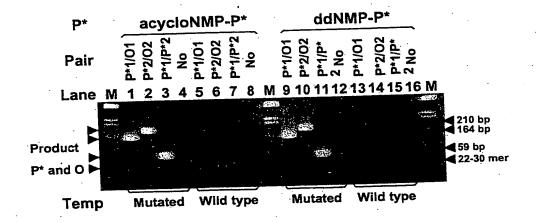




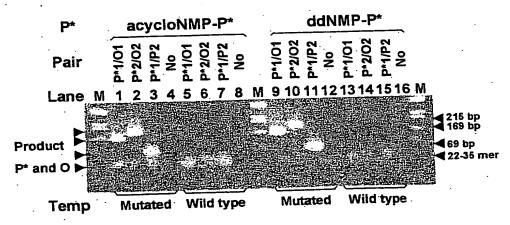
#### **FIG. 18A**



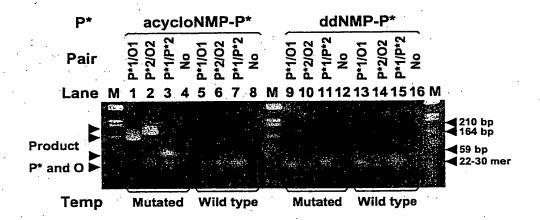
#### **FIG. 18B**



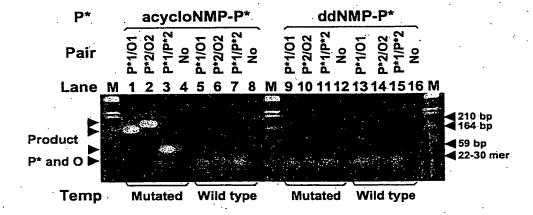
#### **FIG. 18C**



#### **FIG. 18D**



#### **FIG. 18E**



Specific amplification	Nonspecifi	Nonspecific amplification
	I	II
P* 5'.CACA $\mathbf{T}^*$ Template 3'.CGTGT $\mathbf{A}$ GTTG.5'	5'.CACA <b>T</b> * 3'.CGTGT <b>T</b> GTTG.5'	5'.CACA <b>T</b> * 3'.CGTGT <b>T</b> GTTG.5'
Pyrophosphorolysis	Mismatch pyrophosphorolysis	Mismatch pyrophosphorolysis
P* 5′.CACA← Template 3′.CGTGTAGTTG.5′	5'.CACA← 3'.CGTGT <b>T</b> GTTG.5'	5′.CACA← 3′.CGTGT <b>T</b> GTTG.5′
Polymerization	Polymerization	Misincorporation
Product 5'.CACA $T$ CAA> Template 3'.CGTGT $\mathbf{A}$ GTTG.5'	5'.CACAACAA> 3'.CGTGTTGTTG.5'	5'.CACA $oldsymbol{T}_{CAA>}$ 3'.CGTGT $oldsymbol{T}$ GTTG.5'
P* Mutated Template Mutated Product Mutated Frequency 1	Mutated Wild type Wild type 10-5	Mutated Wild type Mutated 3.3x10-11

다 도	
<u>Match</u> Yes	
Template: P* Mate	
Product No	•
Match No	
Template : P* WT:Mut	•

Product Yes

5'...TGGCACA**T\***3'.CGCACCGTGTTGTTGACCGCC.5' 5' GCGTGGCACAACAGCTGGCGG.3' \*AGTTGACC...5

5'.GCGTGGCACATCAACTGGCGG.3'
\*AGTTGACCG...5' 5'...TGGCACAT\*
3'.CGCACCGTGTAGTTGACCGCC.5'

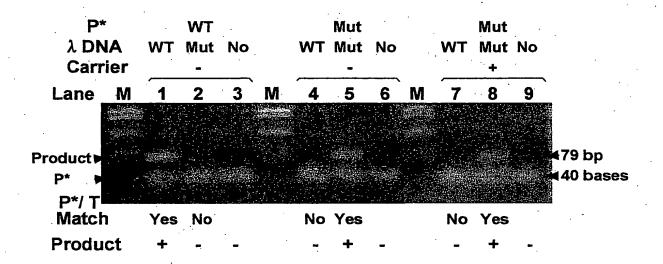
Bi-PAP

5'...TGGCACA*T*CAACTGG...> <...ACCGTGT**A**GTTGACC...s'

\*AGTTGACC...5'

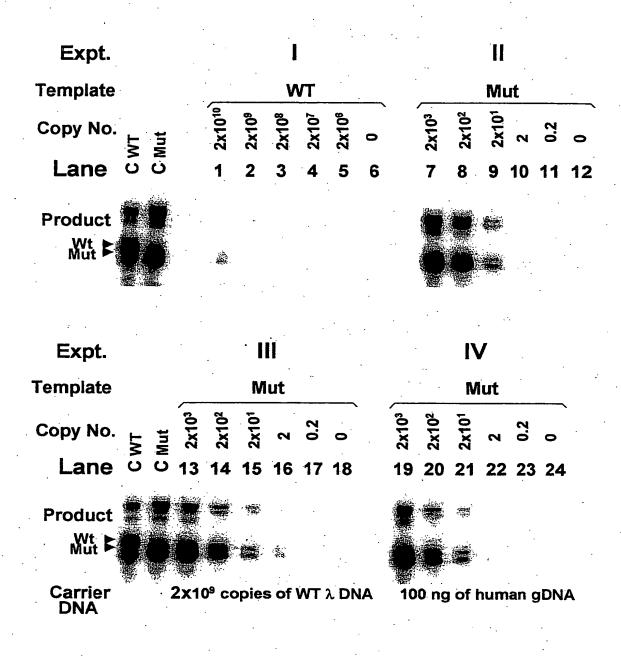
5'...TGGCACAT\*

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**FIG. 20B** 

Pyrophosphorolysis Activated Polymerization (PAP) Qiang LIU et al.. Cont. Appln. filed 12 March 2004 Atty. Docket No. 1954-439 - Page 25 of 33 Pages



**FIG. 21A** 

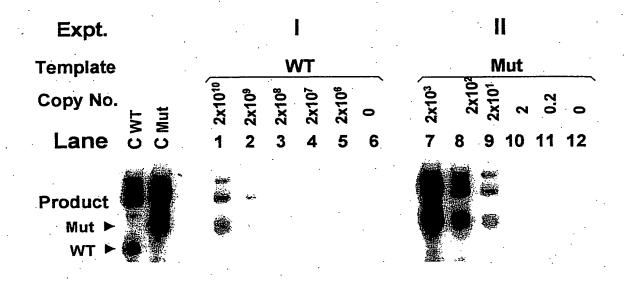


FIG. 21B

**FIG. 21C** 

Mut I

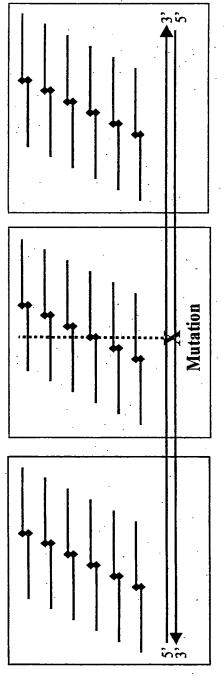


FIG. 22

emplat

\*

Wildty Templa	•	.GCGTGGCACAACTGGCGG.3' .CGCACCGTGTTGTTGACCGCC.5'	<u>Match</u>
	WT	5'TGGCACA <sup>A*</sup> *TGTTGACC5'	Yes
P*	Mut	5'TGGCACA <b>T*</b> * <b>A</b> GTTGACC5'	No
•	Mut	5'TGGCACA <b>G*</b> * <b>C</b> GTTGACC5'	No
	Mut	5'TGGCACA <b>C*</b> * <b>G</b> GTTGACC5'	No
		PAP	<u>Product</u>
	WT	5'TGGCACAACAACTGG> <accgtgt<b>TGTTGACC5'</accgtgt<b>	use <mark>l</mark> aturo la
	Mut	5'TGGCACA <b>T*</b> * <b>A</b> GTTGACC5'	-
P*	Mut	5'TGGCACA <b>G*</b> * <b>C</b> GTTGACC5'	-
	Mut	5'TGGCACA <b>C*</b> * <b>G</b> GTTGACC5'	-

FIG. 23A

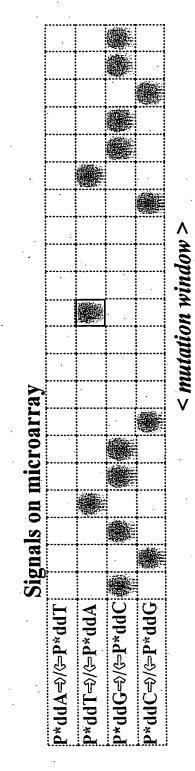
Mutar empla		.GCGTGGCACATCAACTGGCGG.3'.CGCACCGTGTAGTTGACCGCC.5'	<u>Match</u>
	WT	5'TGGCACA <sup>A*</sup> *TGTTGACC5'	No
<b>P</b> *	Mut	5'TGGCACA <b>T*</b> * <b>A</b> GTTGACC5'	Match
	Mut	5'TGGCACA <b>G*</b> * <b>C</b> GTTGACC5'	No
	Mut	5'TGGCACA <b>C*</b> * <b>G</b> GTTGACC5'	No
		PAP	<u>Product</u>
<b>P</b> *	WT	5'TGGCACA <b>A*</b> * <b>T</b> GTTGACC5'	· · -
	Nut	5'TGGCACA <i>T</i> CAACTGG> <accgtgt<b>AGTTGACC5'</accgtgt<b>	
	Mut	5'TGGCACA <b>G*</b> *CGTTGACC5'	-
	Mut	5'TGGCACA <b>C*</b> * <b>G</b> GTTGACC5'	<b>-</b>

FIG. 23B

5'→3' calling of the wild type sample

FIG. 24A

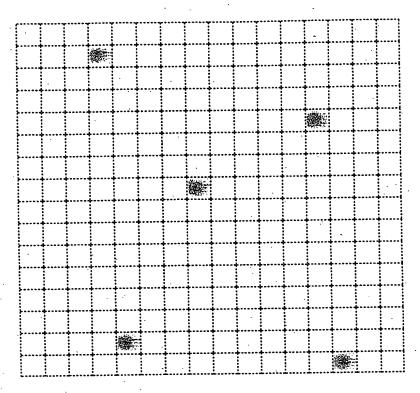
5'-3' strand of the wild type sequence GCGTGGCACA



5'-3' calling of the mutated sample

FIG. 24B

Pyrophosphorolysis Activated Polymerization (PAP) Qiang LiU et al., Cont. Appln. filed 12 March 2004 Atty. Docket No. 1954-439 - Page 32 of 33 Pages



## Assembly of positive signals by one base overlapping

5'...TGGCACA**A**\* **\*T**GTTGACC...5'

5'...GGCACAAC\*
\*GTTGACCG...5'

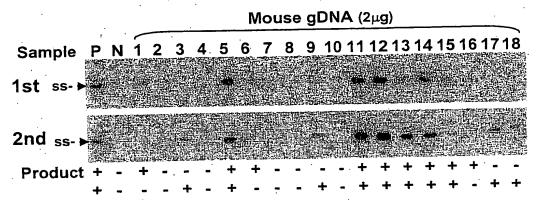
5'...GCACAACA\*
\*TTGACCGC...5'

5'...CACAACA**A\* \*T**GACCGCC...5'

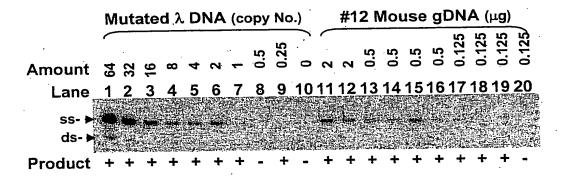
## Reconstruction of the unknown sequence

5' ..... ACAA ..... 3' TGTT ..... 5'





#### **FIG. 26B**



#### **FIG. 26C**